Stone Age hunters contributed adaptive variants to present-day Europeans

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Modern humans have adapted to their local environments over many thousands of years, but how genetic variation contributed to this adaptation remains debated. Using genomes from humans that lived between 45,000 and 7,000 years ago, researchers from the Max Planck Institute for Evolutionary Anthropology in Leipzig have shown that adaptation to local environments has resulted in genetic variants reaching high frequencies in European groups. Interestingly, most of the adaptive variants were present already in an early hunter-gatherer, but not in an early farmer. This suggests that hunter-gatherers, who lived in Europe for thousands of years before the arrival of farmers, were adapted to local environments and contributed adaptive genetic variants to present-day Europeans.

Humans have few genetic differences among individuals, and most of these differences have no effect on phenotype or fitness. The role of local adaptation in population differentiation thus remains unclear.

Using the genome of a 45,000 year old early modern Eurasian from Ust'-Ishim, researchers from the Max Planck Institute in Leipzig investigated the few genetic variants that have large frequency differences between Africans and non-Africans. "When we first heard about the Ust'-Ishim genome we got immediately excited. This individual is extremely useful in that it provides direct information on the genetics of a population that had experienced the out-of-Africa migration, but had not had much time to adapt to Eurasian environments", says Aida Andrés, who led the scientific team.

Her team finds that about 70% of the genomic variants with large frequency differences between Africans and non-Africans are random changes that may have occurred during times of small population size, such as during the migration out of the African continent about 50,000 years ago. Less than 30% of the variants were found to have increased in frequency during or after the colonization of Europe. These are enriched in likely functional parts of the genome such as those that encode proteins and regulate the activity of genes. This suggests that some of them rose in frequency due to positive selection for locally adaptive traits.

Genetically more hunter than farmer

The genomes of additional ancient Europeans provided more detail on local adaptation in Europe. The team showed that an early hunter-gatherer carried more variants that have increased quickly in frequency in Europe than an early farmer. "It is quite striking that, while the Neolithic farming revolution brought a lifestyle to Europe that still persists today, the hunter-gatherers provided the majority of genetic adaptations to the local European environment", says Felix Key, PhD student at the Max Planck Institute in Leipzig and first author of the paper. Eye pigmentation is among the traits likely influenced by hunter-gatherer variants, and the team speculates that these variants may be beneficial in populations living at high latitudes with limited exposure to UV light. However, Key is cautious, commenting that: 'We have to note that our functional understanding of human genetic variants is still limited.'

Andrés sees great potential for this approach in the future: "Combining modern and ancient genomes improves our ability to understand local adaptation. The resolution of studies like ours will keep improving with the growing availability of high-quality ancient genomes." She predicts that "With additional data we are likely to find similar evidence of

genetic adaptations in other continents, too".

More information: Felix M. Key et al. Human adaptation and population differentiation in the light of ancient genomes, *Nature Communications* (2016). DOI: 10.1038/NCOMMS10775

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